

REMARKS/ARGUMENTS

Claims 1-30 are pending. Claims 3-24 have been withdrawn. Claims 1, 2, and 25-30 are under examination. Applicants preserve the right to prosecute any subject-matter withdrawn or canceled by amendment in an appropriate application filed during the pendency of this application.

Species Election

Applicants acknowledge the election of the species renal cancer. Applicants thank the Examiner for setting forth on the record that claims drawn to non-elected species recited in claims 3-24 will be considered once the corresponding generic claim is found allowable.

Applicants aver that claim 1 is allowable for the reasons set forth below. Accordingly, Applicants respectfully request that the Examiner consider claims 3-24 for examination and allow the same to issue in due course.

35 USC § 103(a)

The Examiner has rejected claims 1, 2, 25, 26, and 28 as being obvious in light of Muss et al. in view of Raymond et al. The Examiner alleges that Muss et al. teach a method of treating renal cancer comprising administering interferon alpha (IFN- α) and that Raymond et al. teach a method of treating renal cancer comprising administering CCI-779. The Examiner further alleges that the instant invention would have been obvious by combining the teachings of Muss et al. and Raymond et al. because the documents teach that IFN- α and CCI-779 individually can be used to treat renal cancer.

Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1, 2, 25, 26, and 28 under 35 USC § 103(a).

Claims 1, 2, 25, 26, and 28 are drawn to a method of treating renal cancer by administering a composition comprising CCI-779 (a rapamycin derivative) and IFN- α , and a pharmaceutical pack containing the same. Applicants clearly demonstrate that the combination of CCI-779 and IFN- α is efficacious for treating renal cancer (see, for example, the specification at page 13, Table 1). Applicants demonstrated that the

combination of CCI-779 and IFN- α was able to impart tumor regression as opposed to retarding the growth of tumors, as was observed when CCI-779 and IFN- α were administered individually (see, for example, the specification at page 13, Table 1, and page 14, lines 2-4). Applicants have demonstrated unexpected results because a **synergistic** effect was observed by administering CCI-779 and IFN- α for the treatment of renal cancer (see, for example, the specification at page 13, lines 19-22).

[U]nexpected results . . . are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations [*e.g.* unexpected results] is submitted, the examiner must evaluate the evidence. MPEP § 2141 III.

In addition to unexpected results, Applicants aver there is no expectation of success for combining Muss *et al.* in view Raymond *et al.* to arrive at the instant invention in light of the prior art (FDA Guidelines, *In vivo Drug Metabolism/Drug Interaction Studies – Study Design, Data Analysis, and Recommendations for Dosing and Labeling*, November 1999) and knowledge well-known to persons of ordinary skill in the art. In the FDA guidelines it is clearly recognized that drug-drug interactions are a concern when administering more than one drug (see, for example, page 3). In light of this document and well-known principles of pharmacokinetics, there is no reasonable expectation of success for combining CCI-779 and IFN- α for treating renal cancer. For example, the *in vivo* absorption, distribution, metabolism, and/or elimination of CCI-779 may be partially or completely altered resulting in the drug efficacy being substantially affected or completely abolished in the presence of IFN- α , which displays its intrinsic properties related *in vivo* absorption, distribution, metabolism, and elimination. In light of well-known principles of altered pharmacokinetic and pharmacodynamic properties as a result of drug-drug interactions, Applicants aver that there is no reasonable expectation of success when combining Muss *et al.* in view of Raymond *et al.* to arrive at the instant invention. Further In light of well-known principles of altered pharmacokinetic and pharmacodynamic properties as a result of drug-drug interactions, Applicants aver that the necessary motivation to combine Muss *et al.* in view of Raymond *et al.* is not met in this case.

Applicants also note that all the limitations of the claims are not met by Muss *et al.* in view of Raymond *et al.* For example, claim 25 is drawn to subtherapeutically effective amounts of CCI-779 and IFN- α .

In light of Applicants results and teachings in the prior art, Applicants aver that the invention is not obvious under 35 USC § 103(a) because all of the factors for determining obviousness are not met, the invention displays unexpected results (*e.g.* synergy), and that based on Muss *et al.* in view of Raymond *et al.* there is no reasonable expectation of success and the necessary motivation to combine these documents is not met.

For the reasons set forth above, Applicants aver that the rejection of claims 1, 2, 25, 26, and 28 under 35 USC § 103(a) be withdrawn.

The Examiner has rejected claims 27, 29, and 30 as being obvious in light of Laurent et al. in view of Beuvink et al. The Examiner alleges that Laurent et al. teach a method of treating xenograft tumors comprising administering interferon alpha (IFN- α) and that Beuvink et al. teach a method of treating xenograft tumors comprising administering "RAD001, e.g., 42-O-(2-hydroxy)ethyl rapamycin." The Examiner further alleges that the instant invention would have been obvious by combining the teachings of Laurent et al. and Beuvink et al. because the documents teach that IFN- α and "RAD001, e.g., 42-O-(2-hydroxy)ethyl rapamycin" individually can be used to treat xenograft tumors.

Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 27, 29, and 30 under 35 USC § 103(a).

For the reasons articulated in the response to the rejection predicated on Muss *et al.* in view of Raymond *et al.*, the combination of Laurent *et al.* in view of Beuvink *et al.* also fails to supply the necessary motivation to combine these documents and the reasonable expectation of success required to establish a *prima facie* case of obviousness.


For the reason set forth above, Applicants aver that the rejection of claims 27, 29, and 30 under 35 USC § 103(a) be withdrawn.

In view of the above the remarks/arguments, Applicants respectfully request that the Examiner reconsider and withdraw all outstanding rejections and permit the above pending claims to pass to issue in due course. Applicants also request that the Examiner consider the withdrawn claims and also allow these claims to pass to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to Deposit Account Number 08-3040.

Respectfully submitted,

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